THE ROCKEFELLER UNIVERSITY HOSPITAL
1230 YORK AVENUE · NEW YORK, N.Y. 10021

PHYSICIAN-IN-CHIEF

13 June 1980

Dr. Jan Leschly
Vice President
E. R. Squibb & Sons, Inc.
P.O. Box 4000
Princeton, N. J. 08540

Dear Dr. Leschly:

I am enclosing several reprints on steroid pharmacology which you may be interested in. These reprrints contain the references to the work which I discussed at our recent meeting at the Rockefeller. Copies of the reprints for Dr. Mackaness are also enclosed.

Reprint 1 is an extensive review of a wide variety of biological effects of steroids which fall outside the range of what are generally considered to be "classical" actions of these compounds. I became interested in this subject at the University of Chicago after we had discovered the extraordinary pyrogenic activity of certain 5β steroid metabolites for man. This biological effect of 5β steroids incidentially remains the most species specific steroid action that I know of; so far, out of studies with a dozen animal species, including chimpanzees, it has not been possible to reproduce the pyrogenic action of these compounds experimentally. On the other hand, the fever-producing action of 5β steroids is consistent, has a reproducible pattern (i.e. a latent period of 4-6 hours - peaking at 12-18 hours etc.) and is intense in humans. These steroids have been used at the NIH to determine the bone marrow reserve of leukocytes of patients undergoing radiation therapy for various malignancies since they produce a profound leukocytosis as well as fever in man.

Paper 2 gives additional references to the work I described relating to sex hormone effects on the gastrointestinal tract, including the protective role of estrogens for peptic ulcer disease.

Paper 3 is a report of a simple study we carried out to determine whether estrogens could protect against immune polyarthritis in an animal model of this disease in which an intense disseminated inflammatory joint disease is produced after intradermal injection of complete adjuvant in rats. Estrogens provided a marked anti-inflammatory and suppressive effect on this experimental arthritis. As I indicated, I am sure that

these compounds directly, or through secondary actions that they may exert via their metabolites etc., may well account for the suppressive effect which human pregnancy has on rheumatoid disorders. In this respect Hench was certainly on the right track in attempting to search out the mechanism by which pregnancy protected against exacerbation of rheumatoid arthritis; but he did have his eye on the wrong compounds (bile acids and corticoids). The fortuitous work in the neighboring laboratory of Kendall which provided him with cortisone for his early clinical studies, has certainly led to a great many benefits in clinical medicine, but the beneficial effects of pregnancy on certain inflammatory disorders remain, in my opinion, still unexplained.

I enjoyed the meeting with you and Dr. Mackaness very much and hope that we will have other occasions to meet.

With best regards.

Yours sincerely,

Attallah Kappas, M.D.

Encl.